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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/067,638	04/28/1998	LEX M. COWSERT	ISIS-2960	1414

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EXAMINER

MORAN, MARJORIE A

ART UNIT PAPER NUMBER

1631

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/067,638

Applicant(s)

COWSERT ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 83-87 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 83-87 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/14/05 has been entered. Claims 83-87 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 83-87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

A system for preparing a set of oligonucleotides wherein a computer system FIRST prepares a virtual library of oligonucleotide sequences, then reduces the number of sequences, is new matter. The originally filed claims were directed to methods comprising in silico evaluation of a library of oligonucleotides according to defined criteria (e.g. claim 7) or comprising generating a library of nucleobase compounds in silico according to defined criteria (e.g. claim 8). It is noted that claim 7 and similar original claims did not recite first generating a library of oligonucleotides for evaluation. As many databases of oligonucleotide sequences are

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known in the art (see the NCBI compendium), the library could have been supplied or selected from a database; generation of a virtual library is not inherent. The originally filed specification on page 8 teaches that in a method and system for generating compounds with desired properties, a target nucleic acid sequence is provided or selected, and a library of nucleobase sequences is generated *in silico according to defined criteria*. Original Figure 1 also discloses generating a list of oligonucleotide sequences with desired properties before a step of synthesizing those with desired activities. Original Figure 4 discloses generating oligonucleotide sequences capable of hybridizing to a target sequence. In all cases, the list or virtual library generated is one comprising sequences with selected properties; i.e. one which is already "reduced". Nowhere do the originally filed claims or specification teach preparing or generating a virtual library before any step of selection or reduction. In the response filed 2/14/05, applicant does not point to support by page and line number, or specific Figure element, for the newly recited limitations. As applicant does not provide support, and none is apparent, as set forth above, the claims are rejected for reciting new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Applicant's arguments with respect to claims 83-87 have been considered but are moot in view of the new ground(s) of rejection set forth below.

Claims 83 and 85-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over AGRAFIOTIS et al. (US 5,463,564) in view of HYNDMAN et al. (Biotechniques 20(6): 1090

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(1996)) and NICKERSON et al. (PNAS 87 : 8923 (1990)) and further in view of GRAYBILL et al. (US 6,127,191, filed 12/3/1996).

AGRAFIOTIS, HYNDMAN, and NICKERSON make obvious a system similar to that claimed, as previously set forth and maintained. AGRAFIOTIS, HYNDMAN, and NICKERSON do not specifically teach a computer system which generates a virtual library of oligonucleotide sequences before selection for specific properties.

GRAYBILL teaches an iterative process of selecting compounds with desired properties wherein a virtual library of compounds is generated, then evaluated for specific physical and biological properties (col. 14, lines 40-61).

It would have been obvious to one of ordinary skill in the art to have generated a virtual library of compounds (e.g. oligonucleotide sequences), as taught by GRAYBILL, in the system of AGRAFIOTIS, HYNDMAN, and NICKERSON where the motivation would have been to select compounds for synthesis which best reflect the desired properties, as taught by GRAYBILL (col. 14, lines 54-58). One skilled in the art would reasonably have expected success in combining the teaching of GRAYBILL for generation of a virtual library for screening/reduction in number with the screening/selection of oligonucleotides with desired properties of AGRAFIOTIS, HYNDMAN, and NICKERSON because both GRAYBILL and AGRAFIOTIS teach rational design, selection and synthesis using computer-implemented methods and systems.

Claims 83-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over AGRAFIOTIS et al. (US 5,463,564) in view of HYNDMAN et al. (Biotechniques 20(6): 1090 (1996)), NICKERSON et al. (PNAS 87 : 8923 (1990)), and either ALBERTSEN et al. (US

5,352,775) or CUTTING et al. (US 5,407,796), and further in view of GRAYBILL et al. (US 6,127,191, filed 12/3/1996).

AGRAFIOTIS, HYNDMAN, NICKERSON and ALBERTSEN or CUTTING make obvious a system similar to that claimed, as previously set forth and maintained. None of AGRAFIOTIS, HYNDMAN, NICKERSON, ALBERTSEN or CUTTING specifically teach a computer system which generates a virtual library of oligonucleotide sequences before selection for specific properties.

GRAYBILL teaches an iterative process of selecting compounds with desired properties wherein a virtual library of compounds is generated, then evaluated for specific physical and biological properties (col. 14, lines 40-61).

It would have been obvious to one of ordinary skill in the art to have generated a virtual library of compounds (e.g. oligonucleotide sequences), as taught by GRAYBILL, in the system of AGRAFIOTIS, HYNDMAN, NICKERSON and ALBERTSEN or CUTTING where the motivation would have been to select compounds for synthesis which best reflect the desired properties, as taught by GRAYBILL (col. 14, lines 54-58). One skilled in the art would reasonably have expected success in combining the teaching of GRAYBILL for generation of a virtual library for screening/reduction in number with the screening/selection of oligonucleotides with desired properties of AGRAFIOTIS, HYNDMAN, NICKERSON and ALBERTSEN or CUTTING because both GRAYBILL and AGRAFIOTIS teach rational design, selection and synthesis using computer-implemented methods and systems.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29

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USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 83 and 85-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 55, 56, 58-72, 74-87, and 99-102 of copending Application No. 09/295,463. Although the conflicting claims are not identical, they are not patentably distinct from each other for reasons previously of record. As the claims have not been amended to be patentably distinct and applicant has not presented any arguments with regard to this rejection, the rejection is maintained.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
5/26/05